UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/573,704	02/27/2007	Sylvain Fleury	122481	7110

25944 7590 07/21/2009

OLIFF & BERRIDGE, PLC
P.O. BOX 320850
ALEXANDRIA, VA 22320-4850

EXAMINER	
PARKIN, JEFFREY S	
ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
07/21/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/573,704	FLEURY ET AL.	
	Examiner	Art Unit	
	Jeffrey S. Parkin	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *18-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/20/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Office Action

Status of the Claims

Acknowledgement is hereby made of receipt and entry of the communication filed 10 April, 2009. Claims 1-22 are pending in the instant application. Applicants' election of Group I (claims 1-17 and 22) with traverse is noted. It was argued that a search of both Groups I and II could be made without a serious burden. Applicants' arguments have been carefully considered but are deemed to be unpersuasive for the reasons of record previously set forth. The products of Groups I and II are structurally and functionally different (e.g., polypeptides v. nucleic acids) and do not share a special technical feature. Each group will present unique issues concerning the prior art, enablement, and utility. Accordingly the lack of unity requirement was appropriate and is made **FINAL**. Claims 18-21 are withdrawn from further consideration pursuant to 37 C.F.R. § 1.142(b), as being drawn to a nonelected invention. Claims 1-17 and 22 are currently under consideration.

37 C.F.R. § 1.98

The information disclosure statement filed 20 October, 2006, has been placed in the application file and the information referred to therein has been considered to the extent noted.

35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-17 and 22 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Two separate requirements are set forth under this statute: (1) the claims must set forth the subject matter that applicants regard as their invention; and (2) the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant.

Claim 1 suffers from a number of deficiencies. First, the claim fails to clearly set forth the salient characteristics of the claimed modified polypeptide. The claim references an "immunodominant region", "connecting loop", and the N- and C-helices of a gp41 ectodomain. However the claim fails to identify the corresponding regions in HIV-1 or -2 and the arrangement of these regions with respect to one another. The claim fails to provide any meaningful structural information concerning these regions (i.e., peptide length and corresponding region in HIV-1 gp41). While it is known that gp41 contains amino- and carboxyl-terminal regions (the N- and C-helix regions), these can vary in length depending upon the study. Second, the reference to an "immunodominant" region is confusing. The amino acids corresponding to this region and the properties of this segment are not clearly set forth. What is the source and coding potential of this region? Does the term immunodominant simply reference a strong immune response (e.g.,

humoral or CTL) to a particular region or does it reference an immunodominant/immunosuppressive region (i.e., due to molecular mimicry)? HIV-1 gp41 contains an immunodominant humoral region between the N- and C-helices (corresponding to amino acids 583-609 or 586-620 depending upon the study). However, the claims also require a linker between the N- and C-helices. Does the linker comprise this intervening "immunodominant" region or is it composed of an artificial linker (e.g., SGGRGGS)? Applicants should clearly and unambiguously set forth the structural characteristics of the claimed polypeptide (e.g., A modified human immunodeficiency virus type 1 (HIV-1) gp41 polypeptide comprising an immunodominant region (IDR) of gp41 corresponding to amino acids 583-609, the N-helix region (amino acids 546-579), the C-helix region (amino acids 628-655), and a synthetic linker, wherein the modified polypeptide has the following structure: NH_2-IDR-N-$helix_{583-609}$-linker-C-$helix_{628-655}$-COOH).

Claim 3 is confusing for referencing amino acid residues 603-615 of SEQ ID NO.: 1. The referenced sequence identifier only comprises 140 amino acids. Appropriate clarification is required.

Claim 4 is confusing for referencing amino acid residues 530-542 of SEQ ID NO.: 14. The reference sequence identifier only comprises 137 amino acids. Appropriate clarification is required.

Claim 7 is vague and indefinite for referencing the phrase "most of the amino acid residues". This is a relative term and fails to impart any meaningful structural characteristics upon

the modified polypeptide. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Appropriate correction is required.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Scope of Enablement

Claims 1-17 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The claims are directed toward a poorly defined modified polypeptide comprising an immunodominant region, N-helix, C-helix, and linker. Appropriately drafted claim language directed toward the modified polypeptides of SEQ ID NOS. 8, 17, 18, 19, 20, and 21 would be acceptable.

The legal considerations that govern enablement determinations pertaining to undue experimentation have been clearly set forth. *Enzo Biochem, Inc.*, 52 U.S.P.Q.2d 1129 (C.A.F.C. 1999). *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988).

Ex parte Forman 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

1) The disclosure fails to provide adequate guidance pertaining to the coding potential of the "immunodominant" region. Which amino acids comprise this region? Is this region composed of humoral epitopes, CTL epitopes, or T-helper epitopes?

2) The disclosure fails to provide sufficient guidance pertaining to suitable mutations that prevent cross-reactivity with host B- or T-cell epitopes (see claims 9 and 10). The disclosure fails to identify suitable cross-reactive epitopes present in the modified polypeptide and it fails to identify suitable mutations that will abrogate immunological cross-reactivity while maintaining the desirable polypeptide properties.

3) The disclosure fails to provide sufficient guidance pertaining to suitable mutations that improve the solubility of the modified polypeptide (see claim 12). Which amino acid additions, deletions, or substitutions will produce a polypeptide with the desired properties?

4) The claim breadth is considerable and encompasses a large number of mutants comprising amino acid substitutions,

additions, and deletions. However, the disclosure fails to provide a detailed structural/functional analysis of polypeptide mutants that retain the desired properties.

5) The disclosure fails to provide a sufficient number of working embodiments. Considering the unpredictability associated with mutagenic studies, multiple working examples would be required to enable the full breadth of the patent protection desired.

6) The state-of-the-art teaches that single amino acid additions, deletions, or substitutions can abrogate polypeptide activity (i.e., antigen-antibody binding interactions). Thus considerable guidance would be required from the specification identifying suitable mutants.

When all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation from the skilled artisan to practice the invention in a manner commensurate in scope with the claims. Applicants may obviate the rejection by amending the claim language as suggested *supra*.

Enablement

Claim 22 is rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 22 is drawn toward a vaccine composition comprising the modified polypeptide. The term "vaccine" is art-recognized and encompasses a therapeutic or prophylactic immune response.

The legal considerations that govern enablement determinations pertaining to undue experimentation have been clearly set forth. *Enzo Biochem, Inc.*, 52 U.S.P.Q.2d 1129 (C.A.F.C. 1999). *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988). *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

1) The state-of-the-art vis-à-vis HIV vaccine development has been characterized by repeated failure (Desrosiers, 2004; Burton, 2004; Gallo, 2005; Walker and Burton, 2008). Several factors have contributed to the lack of success including the following: 1) The quasispecies nature of HIV infection leads to rapid immune evasion and escape due to neutralization resistance. 2) HIV is capable of down-regulating major histocompatibility class I (MHC) molecules from the surface of infected cells thereby rendering them resistant to CTL-mediated cytolysis. 3) HIV selectively targets and destroys $CD4^+$ T-helper cells thereby hampering the ability of the immune system to mount a meaningful response. 4) Current animal models are not predictive of clinical efficacy. 5) The correlates of human protection remain to be elucidated. 6) The appropriate immunogen(s), formulations, adjuvants, routes of administration,

and immunization regimens that will lead to a protective or therapeutic outcome remain to be elucidated. 7) HIV is capable of integrating into the host's chromosome where it may actively replicate or enter a quiescent phase. Thus, any given immune response will need to maintain high titers of neutralizing activity.

2) The disclosure fails to provide adequate guidance pertaining to the coding potential of the "immunodominant" region. It is not readily manifest which amino acids correspond to this region.

3) The disclosure fails to provide sufficient guidance pertaining to suitable mutations that prevent cross-reactivity with host B- or T-cell epitopes. The disclosure fails to identify cross-reactive epitopes and fails to provide any further mutagenic analyses of these regions.

4) The disclosure fails to provide sufficient guidance pertaining to suitable mutations that improve the solubility of the modified polypeptide. It is not readily manifest which mutations will produce a modified polypeptide with the desired properties.

5) The disclosure fails to provide adequate guidance pertaining to suitable vaccine formulations, adjuvants, routes of administration, and immunization regimens. The claim fails to identify a suitable immunogen, vaccine formulation, and immunization regimen.

6) The disclosure fails to provide any working embodiments. Considering the unpredictability of the prior art, a working embodiment providing some sort of therapeutic or prophylactic outcome would be required.

7) The claim breadth is considerable and encompasses a large number of mutants comprising amino acid substitutions, additions, and deletions (see items 2-4 *supra*).

Accordingly, when all of the aforementioned factors are considered *in toto*, it would clearly require undue experimentation from the skilled artisan to practice the claimed invention. Applicants may obviate the rejection by directing the claim language toward an "immunogenic composition" comprising the modified polypeptide of claim 1.

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Larry R. Helms, can be reached at (571) 272-0832. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Applicants are reminded that the United States Patent and Trademark Office (Office) requires most patent related correspondence to be: a) faxed to the Central FAX number (571-273-8300) (updated as of July 15, 2005), b) hand carried or delivered to the Customer Service Window (now located at the Randolph Building, 401 Dulany Street, Alexandria, VA 22314), c) mailed to the mailing address set forth in 37 C.F.R. § 1.1 (e.g., P.O. Box 1450, Alexandria, VA 22313-1450), or d) transmitted to the Office using the Office's Electronic Filing System. This notice replaces all prior Office notices specifying a specific fax number or hand carry address for certain patent related correspondence. For further information refer to the Updated Notice of Centralized Delivery and Facsimile Transmission Policy for Patent Related Correspondence, and Exceptions Thereto, 1292 Off. Gaz. Pat. Office 186 (March 29, 2005).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

/Jeffrey S. Parkin/
Primary Examiner, Art Unit 1648

18 July, 2009